Reviewer's report

Title: Evaluating regional blood spinal cord barrier dysfunction following spinal cord injury using longitudinal dynamic contrast-enhanced MRI: application in mouse

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Reviewer: David Hackney

Reviewer's report:

The authors report a detailed investigation of early blood spinal cord barrier response to mechanical injury. The technical quality of the images is excellent. However, the manuscript seems to be very short on data, and reads more as an extended description of methods, with little in the way of results. The heart of the data would appear to be the temporal response of the BSCB after injury. This data is summarized in a few figures, and seem to show an early dramatic increase in BSCB permeability, with subsequent reductions in ktrans. However, the remainder of the manuscript does not contribute to this evaluation. Instead, there are subjective and qualitative descriptions of findings, with little in the way of criteria. Thus, it is impossible to determine whether the inferences about primary versus secondary injury are correct, or supported by their results.

The manuscript would benefit from an extensive rewrite. The authors need to decide what data they wish to report, presumably the BSCB permeability data, then focus their presentation on these results.

On the rewrite, it would be important to edit the manuscript so that only the important information is included. The extended description of the permeability study seems to report a standard implementation of DCE. If there is something unique here the authors should make it clear what they believe this to be. If it is a standard implementation, then only a brief summary and reference are needed.

The authors have presented the BSCB permeability data from measures of 6 images approximately centered on the injury site. However, it is not clear how they identified the injury site. This approach also assumes that the effects of the injury extended only on these images, with no effects farther away. If this is not true, then this approach underestimates the extent of the lesion, and obscures the temporal evolution of the injury.

By imaging only twice, they assume they can characterize the permeability of the BSCB. But this will not produce accurate results if the wash in and wash out phases are different than they assume.

Omit figure 2.

Figure 3 displays the interesting finding of hyperintensity in the corticospinal track rostral, but not caudal, to the injury site. Since one might expect more rapid antegrade than retrograde degeneration, was this a reproducible finding, or
observed only in the illustrated cord?

Figures 4, 5, and 6 can be omitted.

Legend for figure 8 appears to describe figure 9.

The legend for figure 9 apparently describes the images displayed in figure 10. The legend states that white arrows denote vasculature whose BSCB became leaky due to secondary inflammatory processes. Unfortunately, the authors do not state how they concluded this. What in the image indicates BSCB damage? How do they know it is due to inflammatory secondary injury?

The legend for figure 10 apparently describes figure 11. The authors do not explain why this is included as well as figure 10, both appear to present the same findings.

The legend for figure 11 apparently describes figure 12. This portion of the study would benefit greatly from a more quantitative approach to analyzing the immunohistochemistry results.

The legend for figure 12 apparently describes figure 13.

The legend for figure 13 apparently describes figure 14.

The legend for figure 14 apparently describes figure 15.

The legend for figure 15 apparently describes figure 16.

Given the extensive revisions required, it would be difficult to predict an overall score after these have been completed.